# Effects of expectations on pain perception and learning in fibromyalgia patients

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1. To assess whether the extinction of pain expectations differs between fibromyalgia patients and healthy participants \* If so, to assess whether this is due to stronger expectancy-based modulation of pain perception and/or a stronger confirmation...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Observational non invasive

# Summary

### ID

NL-OMON45539

**Source** ToetsingOnline

**Brief title** fibromyalgia and cognition

### Condition

• Other condition

**Synonym** fibromyalgia

#### **Health condition**

pijnstoornissen

### **Research involving**

Human

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### **Sponsors and support**

Primary sponsor: Universiteit Leiden Source(s) of monetary or material Support: NWO

### Intervention

Keyword: expectations, extinction learning, fibromyalgia, perception

### **Outcome measures**

#### **Primary outcome**

Pain-learning task:

- Cue effect on reported pain during the extinction phase
- Cue effect on heat-evoked skin-conductance responses during the extinction

phase

- Confirmation bias on learning rate during the extinction phase

Visual-discrimination task:

- Reported unpleasantness and discrimination accuracy of visual stimulation, as

a function of stimulation intensity

#### Secondary outcome

- Learning rate on the reward-learning task (to assess the specificity of

potential learning abnormalities in the patient group to aversive learning

situations)

- Temporal summation phenomenon
- Overall sensitivity to heat pain (self-reported pain and skin-conductance

responses to contact heat)

- Questionnaire scores (see section 5.2)

# **Study description**

#### **Background summary**

Chronic pain is one of the most burdensome health conditions worldwide, affecting approximately 20% of the world population 1. Unlike acute pain, chronic pain serves no biological purpose, has long-lasting disabling effects, and is associated with an array of psychological, social and economic costs 2-5. Many cases of chronic pain remain medically unexplained as they lack a clear peripheral pathology. Interestingly, recent neuroimaging studies have revealed altered brain structure and function in chronic-pain patients 6-8. This suggests that alterations at the brain level, and of related \*top-down\* psychological/cognitive processes\*including fear, avoidance, expectations, memory and learning\*may play an important role in the development and maintenance of chronic pain 9-11. However, empirical studies examining (aberrant) cognitive processes in chronic pain patients are rare; hence the contribution of psychological influences to the pathology of chronic pain is still largely unknown.

Studies in healthy participants, on the other hand, have provided ample evidence that pain perception can be strongly modulated by psychological processes, such as expectations and attention 12,13. In the proposed research, we will focus on the effects of expectations. Multiple studies have shown that expectations about pain\*induced by previous experiences and/or instructions\* result in the adjustment of pain responses toward the expected pain level 14-16. Moreover, the effects of prior expectations on pain often persist, or even grow over time, even when these expectations are not, or no longer, valid 16-19. That is, expectations about pain can become \*self-fulfilling prophecies\* that are resistant to extinction. We recently demonstrated two, not mutually exclusive, mechanisms promoting such self-reinforcing expectancy effects on pain in healthy participants 20. First, we found that participants\* pain perception was biased toward their expected pain levels, creating a positive feedback loop between expectations and pain perception. Second, participants showed a \*confirmation bias\* in learning, such that expectation updating was stronger (i.e., learning rate was higher) when new pain experiences confirmed, than when they disconfirmed, prior expectations. Both of these effects varied substantially across healthy individuals 20.

Self-reinforcing expectancy effects on pain perception may promote the development and maintenance of a chronic pain syndrome. Indeed, the inability to extinguish pain memories has been proposed as a defining aspect of chronic pain 21,22. Furthermore, a few studies have demonstrated impaired cue-pain contingency learning in chronic pain patients, with a particular impairment in safety learning 9,11, which may reflect a confirmation bias. However, these studies focused on the acquisition of pain expectations and did not examine the

(resistance to) extinction. Chronic pain has also been related to aberrant perceptual processing 23, but the specific roles of perceptual and learning processes in the development and maintenance of chronic pain remain to be clarified 24. In the proposed research, we will address these issues, by examining the effects of prior cue-based expectations on both pain perception and extinction learning in chronic pain patients compared to healthy control participants. We will focus on fibromyalgia, one of the most common types of chronic pain conditions that is characterized by widespread musculoskeletal pain, often without a clear medical explanation.

In addition to assessing expectancy effects of pain perception and pain-related learning, we will also examine potential differences between fibromyalgia patients and healthy participants in sensitivity to non-painful sensory (visual) stimulation. In addition to greater pain sensitivity, reduced tolerance to innocuous auditory, visual, olfactory, and tactile stimuli has been reported in fibromyalgia patients 25-30. These observations have mostly been obtained from self-report questionnaires about daily life sensations. In agreement with the self-report data, significant brain-related abnormalities have been observed in response to visual and auditory stimuli in fibromyalgia patients 23,25,31,32. These multisensory processing abnormalities may reflect an important pathophysiological mechanism underlying pain in fibromyalgia patients. However, specific measures about the magnitude and reliability of such alterations, obtained in a controlled experimental setting, are currently lacking.

### Study objective

1. To assess whether the extinction of pain expectations differs between fibromyalgia patients and healthy participants

\* If so, to assess whether this is due to stronger expectancy-based modulation of pain perception and/or a stronger confirmation bias in expectation updating 2. To assess whether fibromyalgia patients and healthy participants differ in their sensitivity to visual stimulation and/or in the ability to discriminate different intensities of visual stimulation

### Study design

The proposed study will use a case-control design, comparing a group of 30 fibromyalgia patients to a group of 30 healthy control participants matched on age, gender, and educational level. We will collect behavioral and physiological (skin conductance) data from all participants, during a number of experimental tasks (see section 5.2). All tasks will be administered in the LUMC, and this will take approximately 2 hours in total (including a short break). In addition, all participants will complete several questionnaires (see section 5.2) at home via Qualtrics, prior to the test day, which will take 20-30 minutes.

#### Study burden and risks

There are no serious risks associated with participation in this study. We have ample experience with thermal stimulation, it is without major side effects. The used equipment is limited to avoid thermal burns to the skin. A red discoloration of the skin can occur after testing, which usually resolves within several hours.

Participants will receive monetary compensation for their time, but there is no other direct benefit to the participants from this proposed research. However, the potential knowledge gained from this study has greater benefits to society: Although several types of chronic pain disorders are believed to arise, at least partly, from dysfunctional neurocognitive processes, there has been a paucity of empirical studies investigating this idea. The detection and characterization of potential learning and perception biases in fibromyalgia patients in the proposed study can help understand the mechanisms underlying the development and maintenance of this chronic-pain disorder, which may eventually contribute to the development of new treatment protocols.

# Contacts

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# **Trial sites**

# Listed location countries

Netherlands

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# **Eligibility criteria**

#### Age

Adults (18-64 years) Elderly (65 years and older)

### **Inclusion criteria**

- Female

- 18-65 years old
- Able to give written informed consent;Additional inclusion criterion for patient group:

- Diagnosed with fibromyalgia by a rheumatologist, according to the ACR criteria (1990 or 2010)

# **Exclusion criteria**

At least one of the following criteria for all subjects:

- Significant intellectual or learning disabilities
- Visual or hearing disabilities (contacts or glasses are ok)
- Obesity (body mass index > 30 kg/m2)
- Medical disease such as pulmonary, renal, liver, cardiac, gastro-intestinal, vascular disease
- History of chronic alcohol or illicit drug use
- Regular use of opioids (tramadol, oxycodone, morphine, fentanyl, etc)
- Pregnancy

- Use of painkillers or other \*rescue\* (irregular) medication < 48 hours before the experiment

- History of epilepsy
- Abnormal amount of current pain (e.g., due to recent injury or surgery)
- Any other condition that, as judged by the investigator, is expected to interfere with optimal study participation, or could confound the results of the study ;Additional exclusion criterion for patient group:

- Presence of any other pain syndrome, other than fibromyalgia (such as osteoarthritis, polyneuropathy, rheumatic disease, etc)

# **Study design**

# Design

Study type: Intervention model: Observational non invasive Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

### Recruitment

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NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	18-07-2017
Enrollment:	60
Туре:	Actual

# **Ethics review**

Approved WMO	
Date:	20-06-2017
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

# **Study registrations**

# Followed up by the following (possibly more current) registration

No registrations found.

# Other (possibly less up-to-date) registrations in this register

No registrations found.

### In other registers

Register CCMO **ID** NL61349.058.17